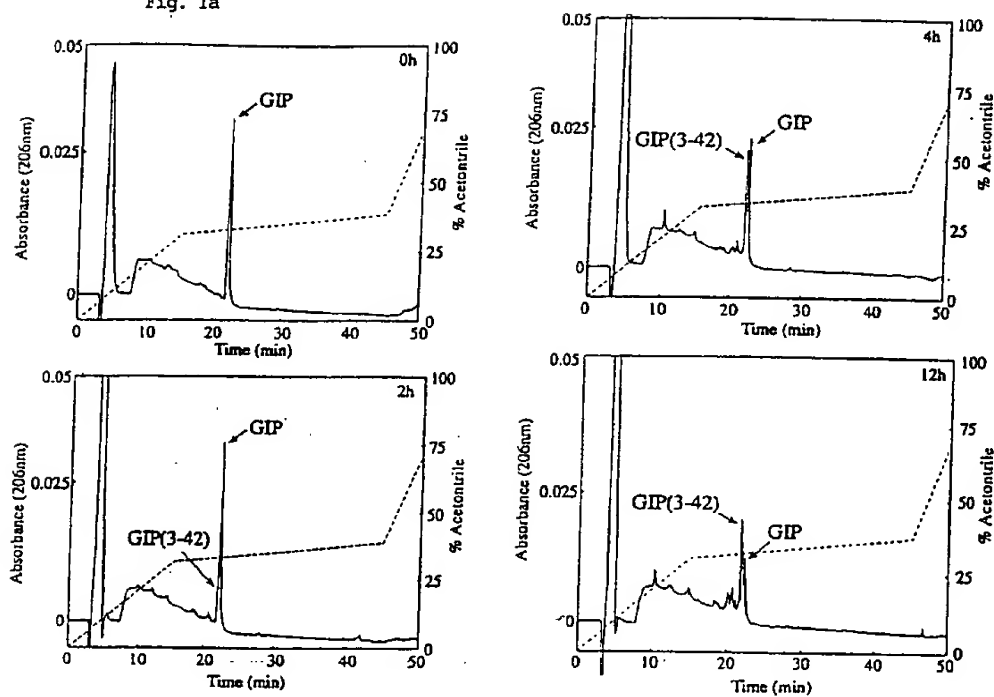


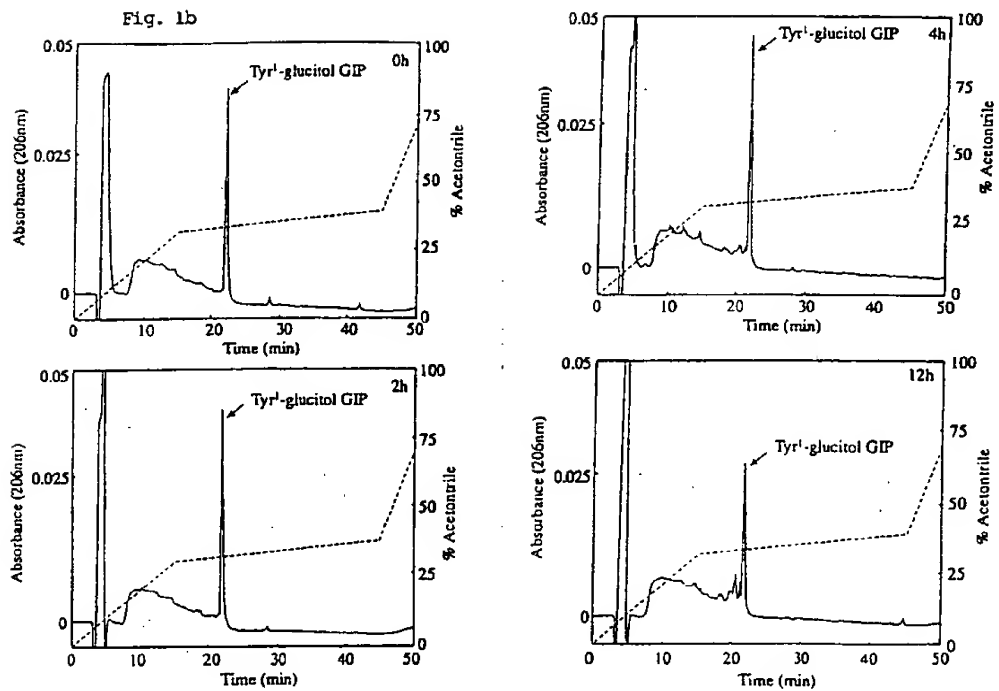
WO 00/58360

PCT/GB00/01089

1/32

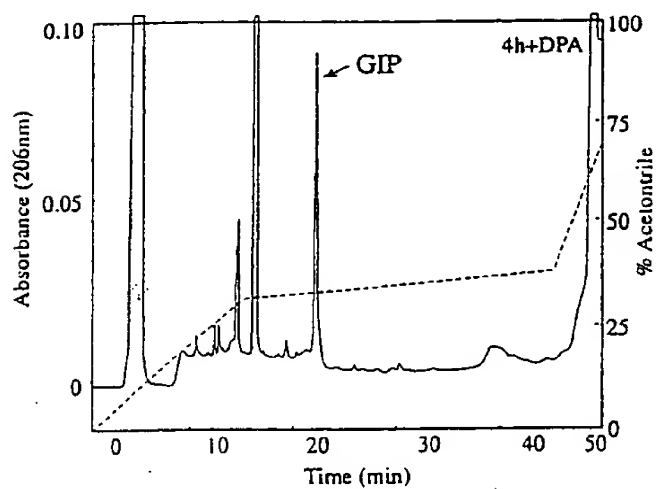
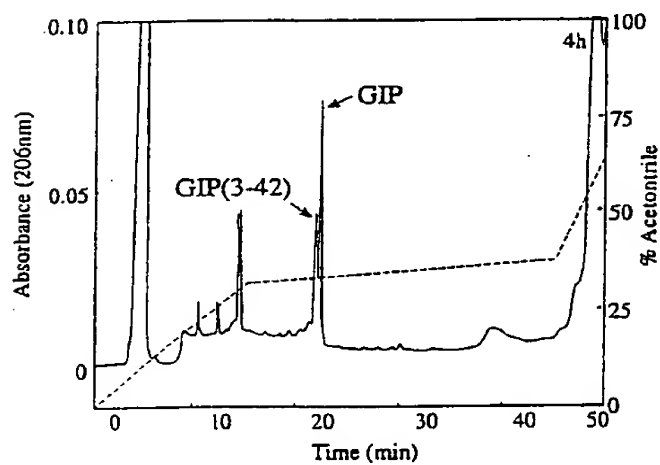
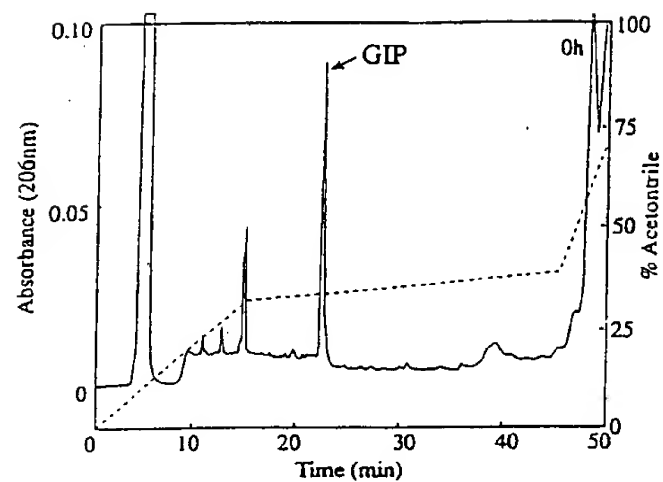
Fig. 1a





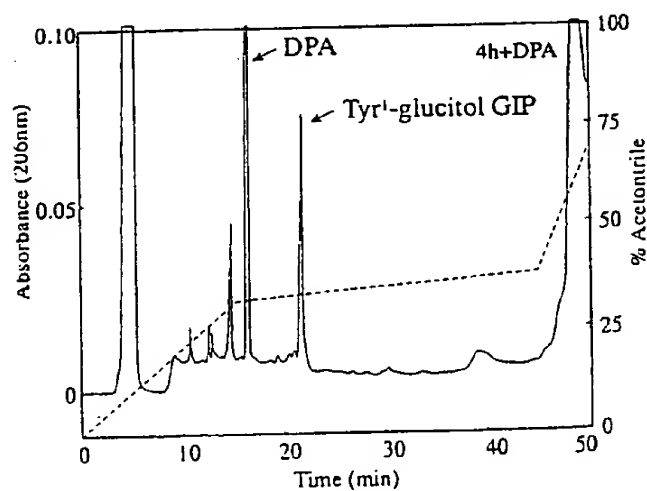
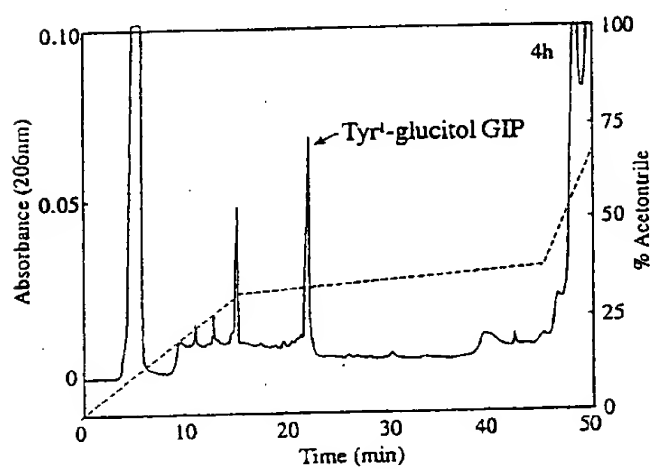
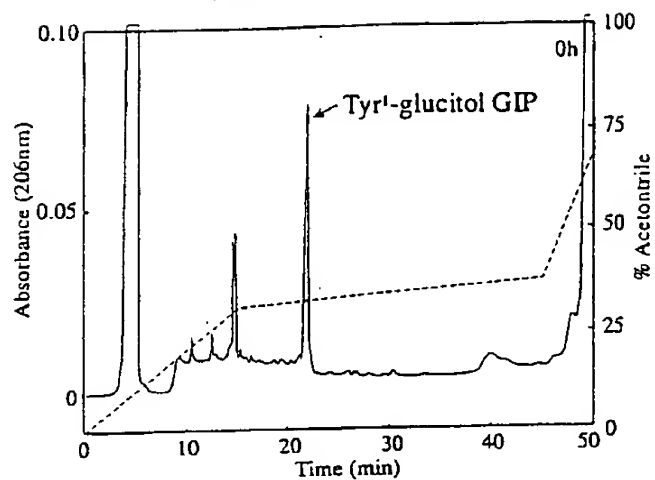
3/32

Fig. 2a

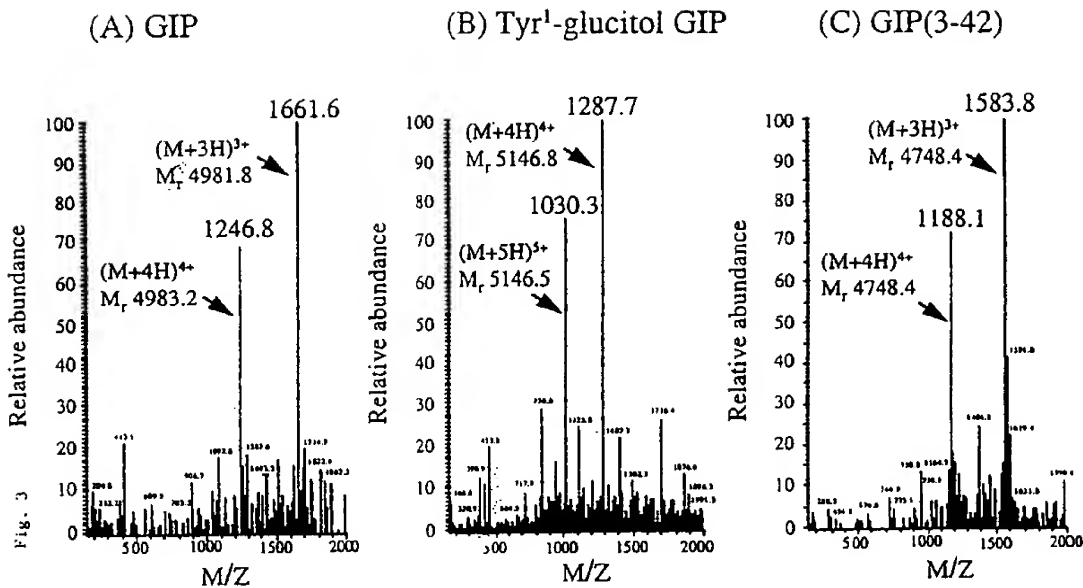


4/32

Fig. 2b

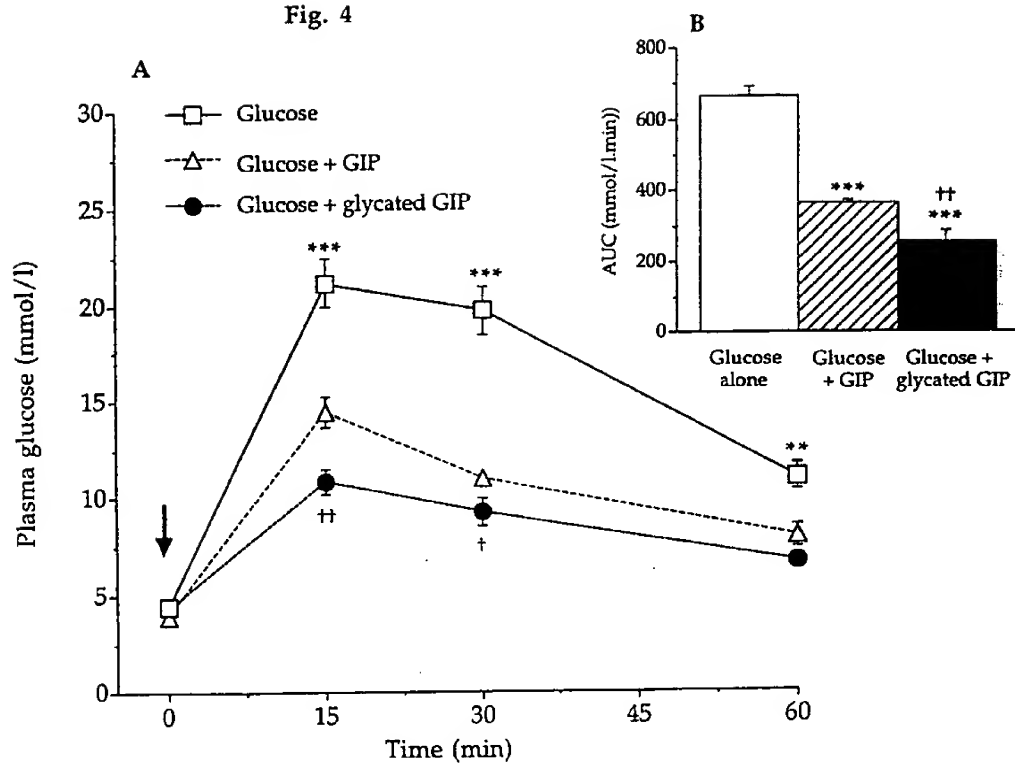


5/32

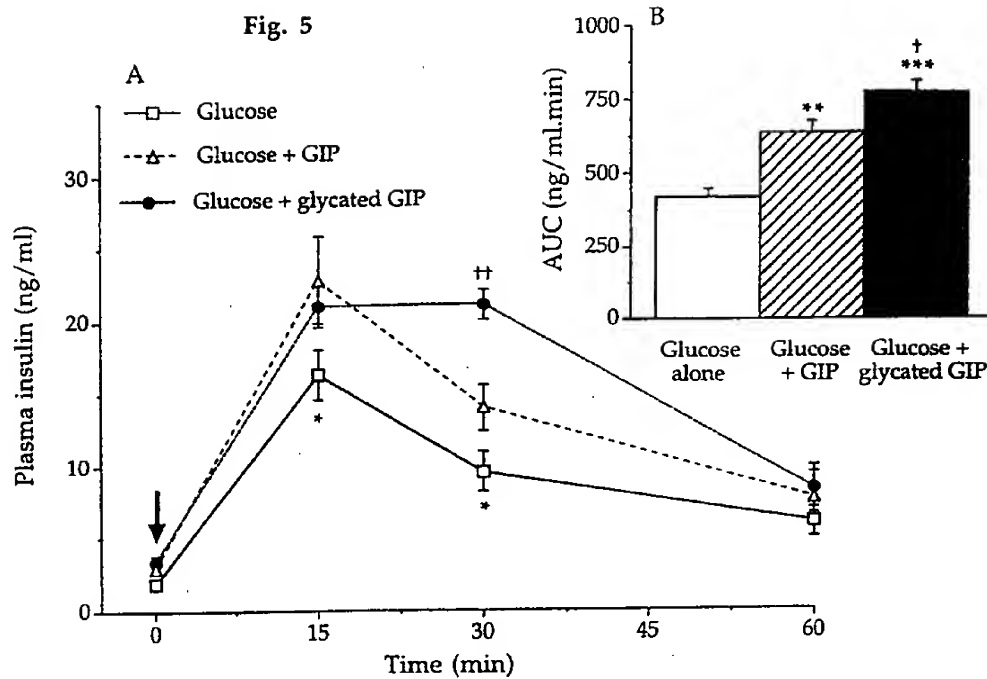


6/32

Fig. 4



7/32



8 / 32

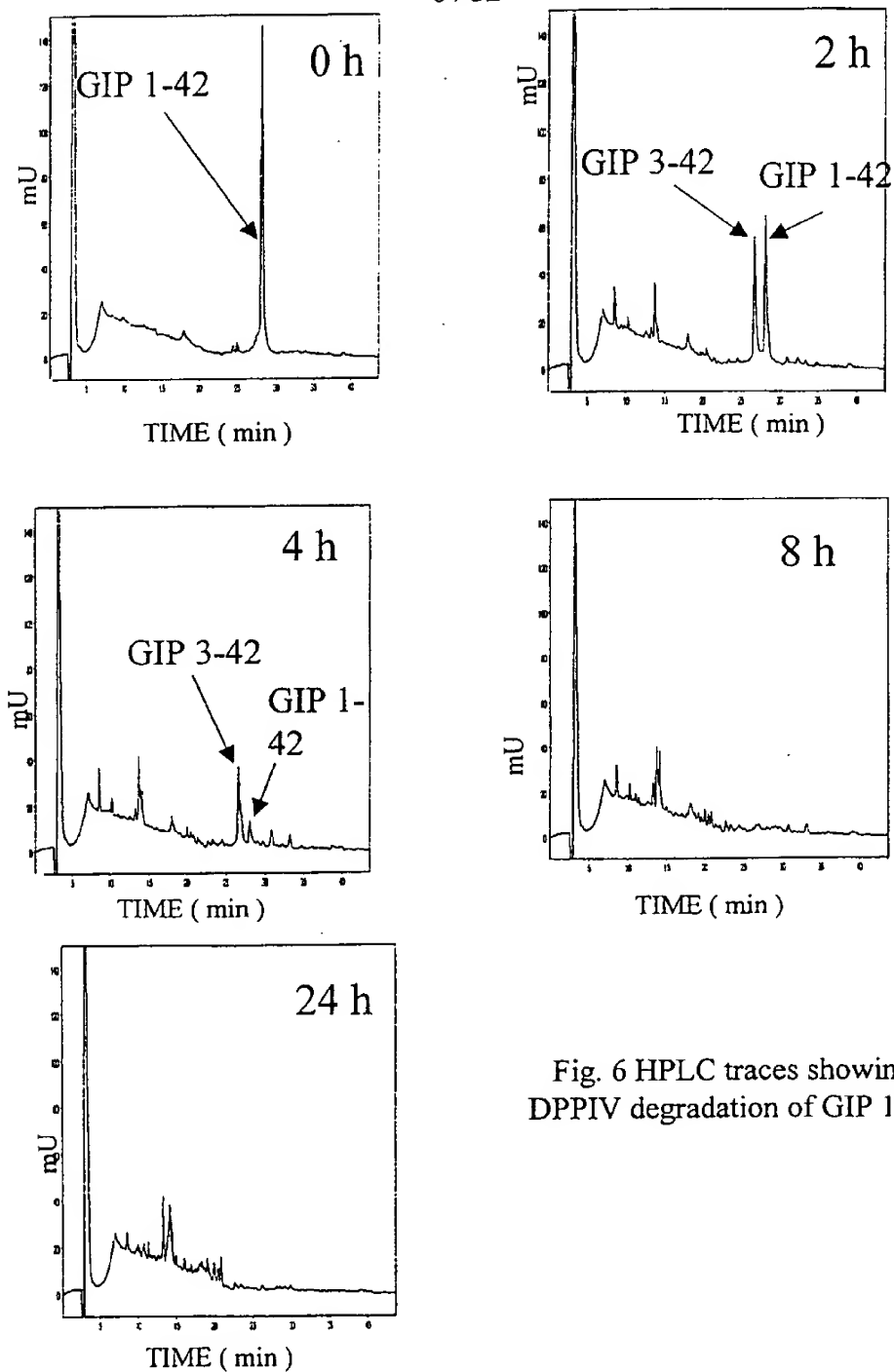


Fig. 6 HPLC traces showing
DPPIV degradation of GIP 1-42

9/32

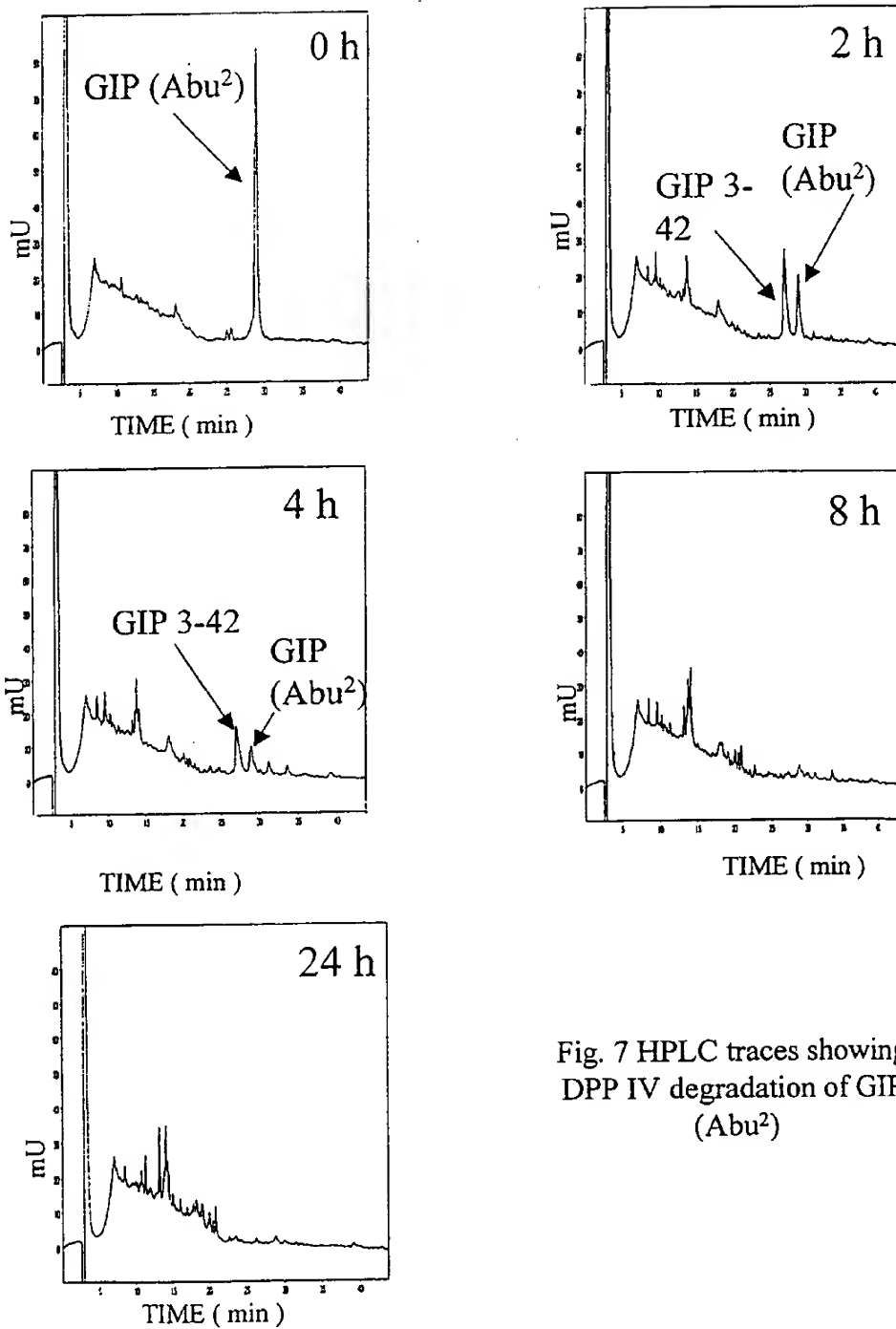


Fig. 7 HPLC traces showing
DPP IV degradation of GIP
(Abu²)

10/32

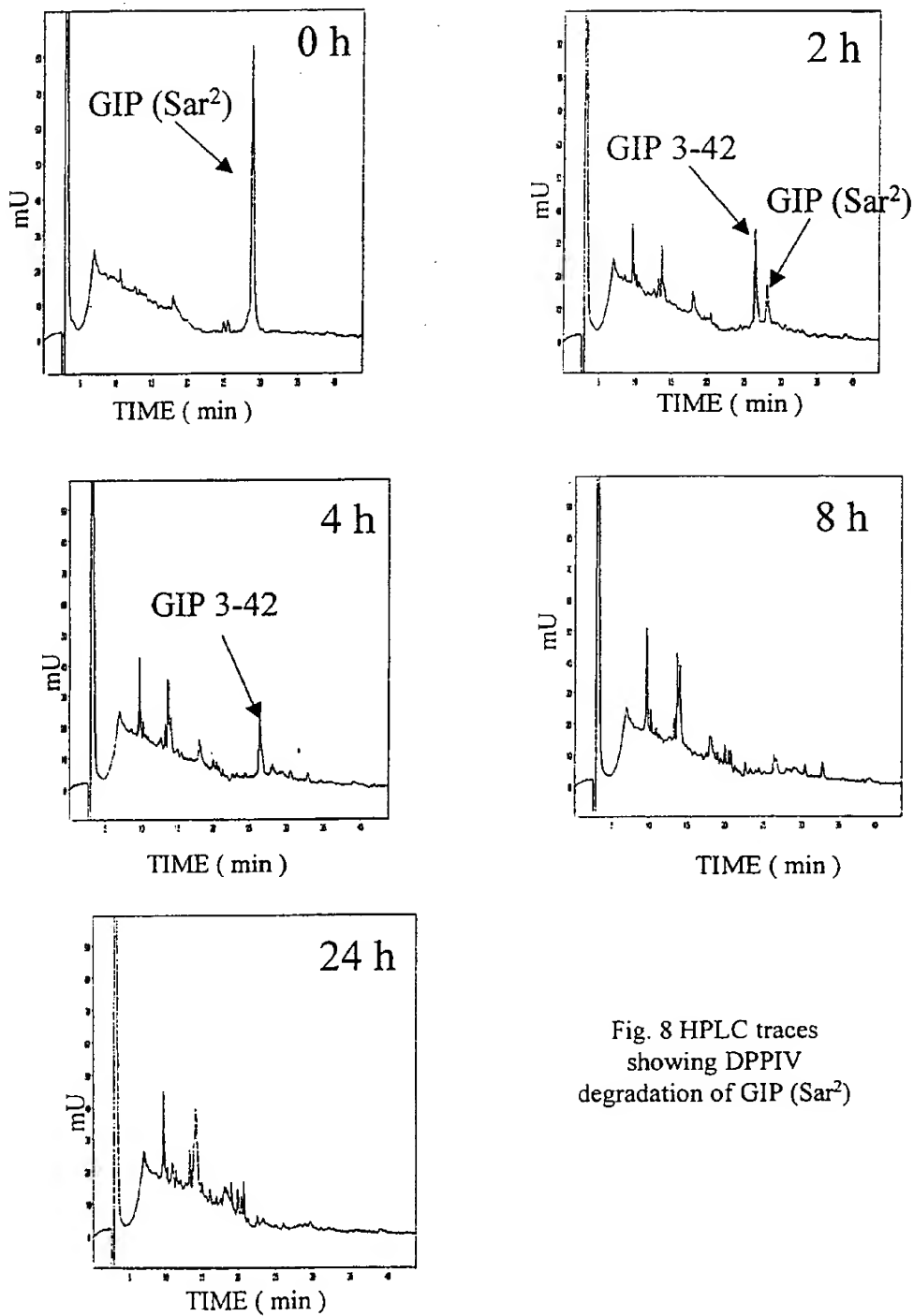


Fig. 8 HPLC traces
showing DPPIV
degradation of GIP (Sar²)

WO 00/58360

PCT/GB00/01089

11 / 32

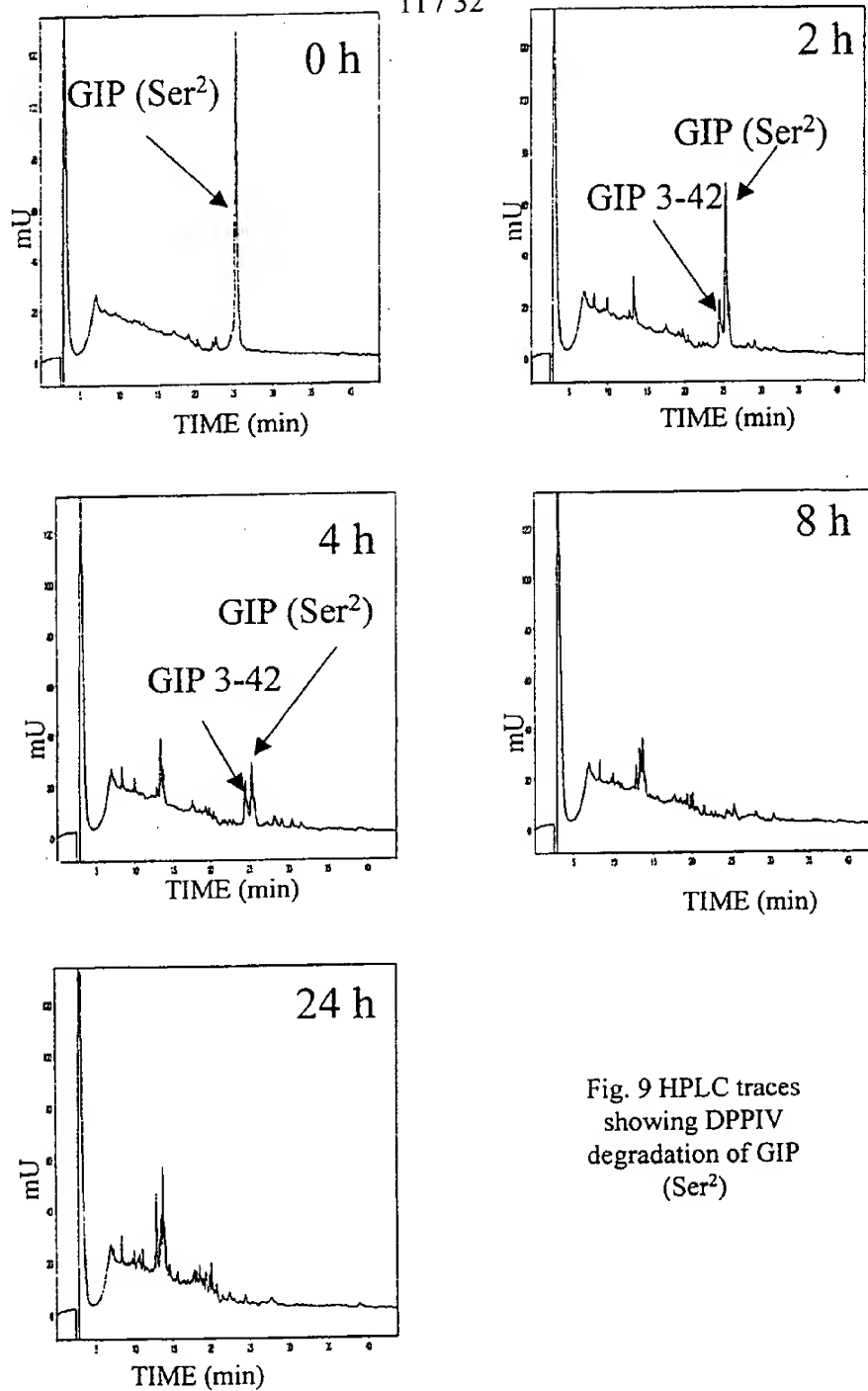


Fig. 9 HPLC traces
showing DPPIV
degradation of GIP
(Ser²)

12 / 32

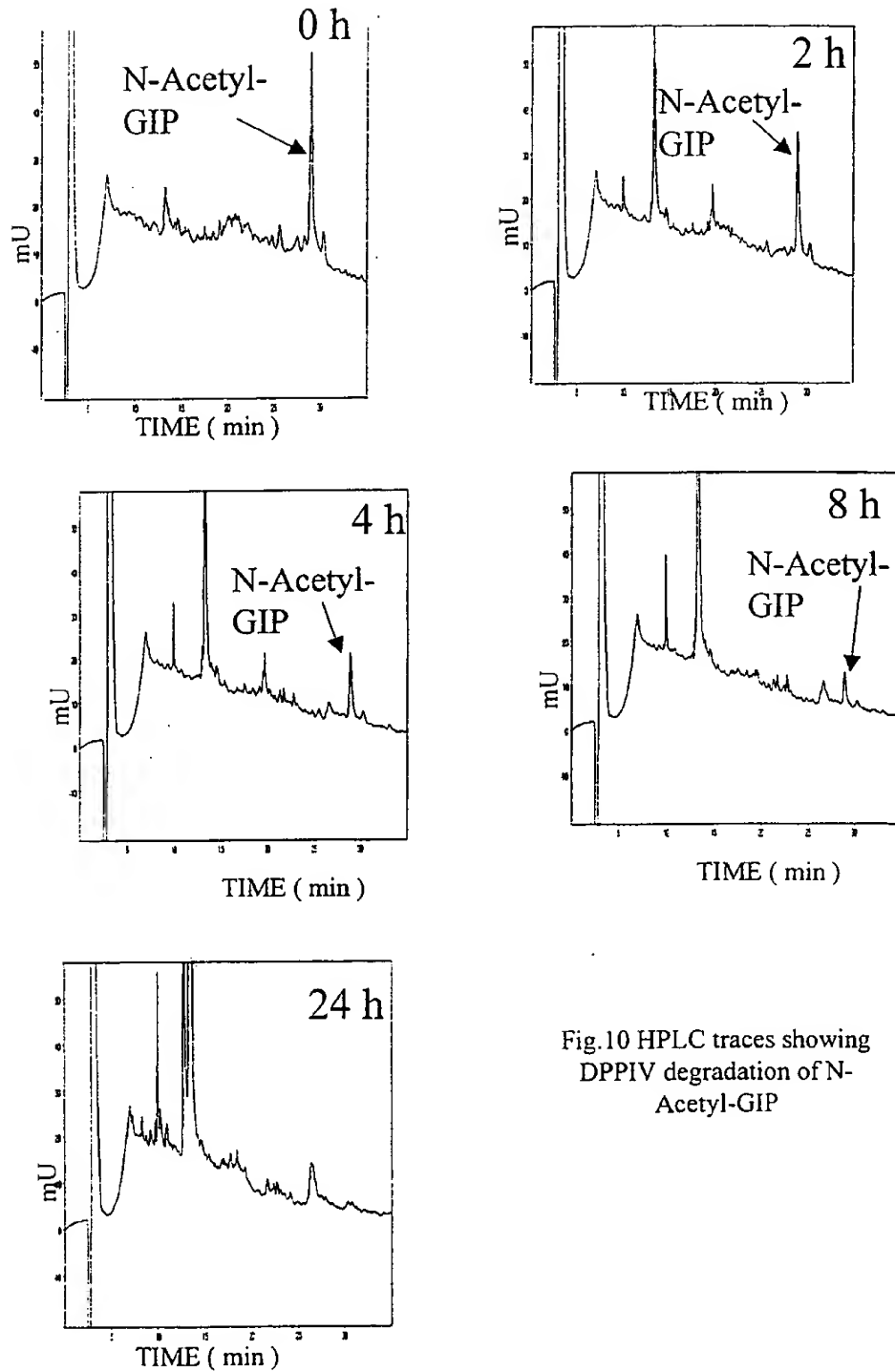


Fig.10 HPLC traces showing
DPPIV degradation of N-
Acetyl-GIP

13 / 32

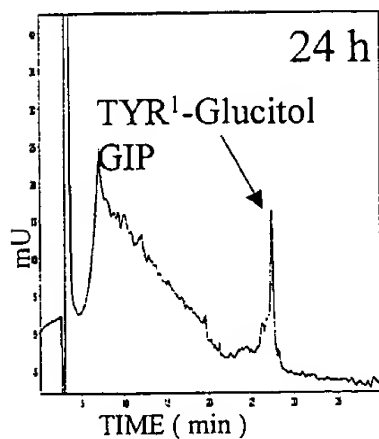
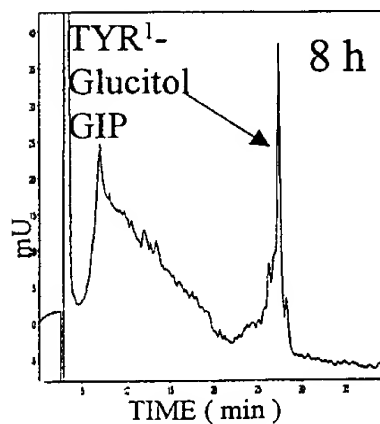
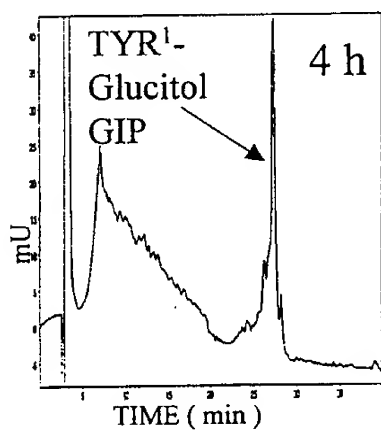
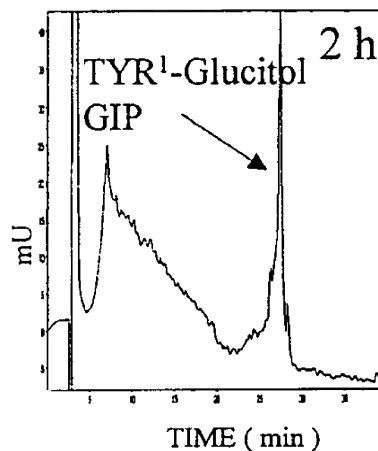
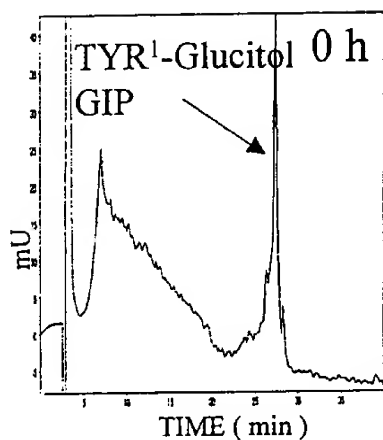


Fig. 11 HPLC traces showing
DPPIV degradation of
glycated GIP

14 / 32

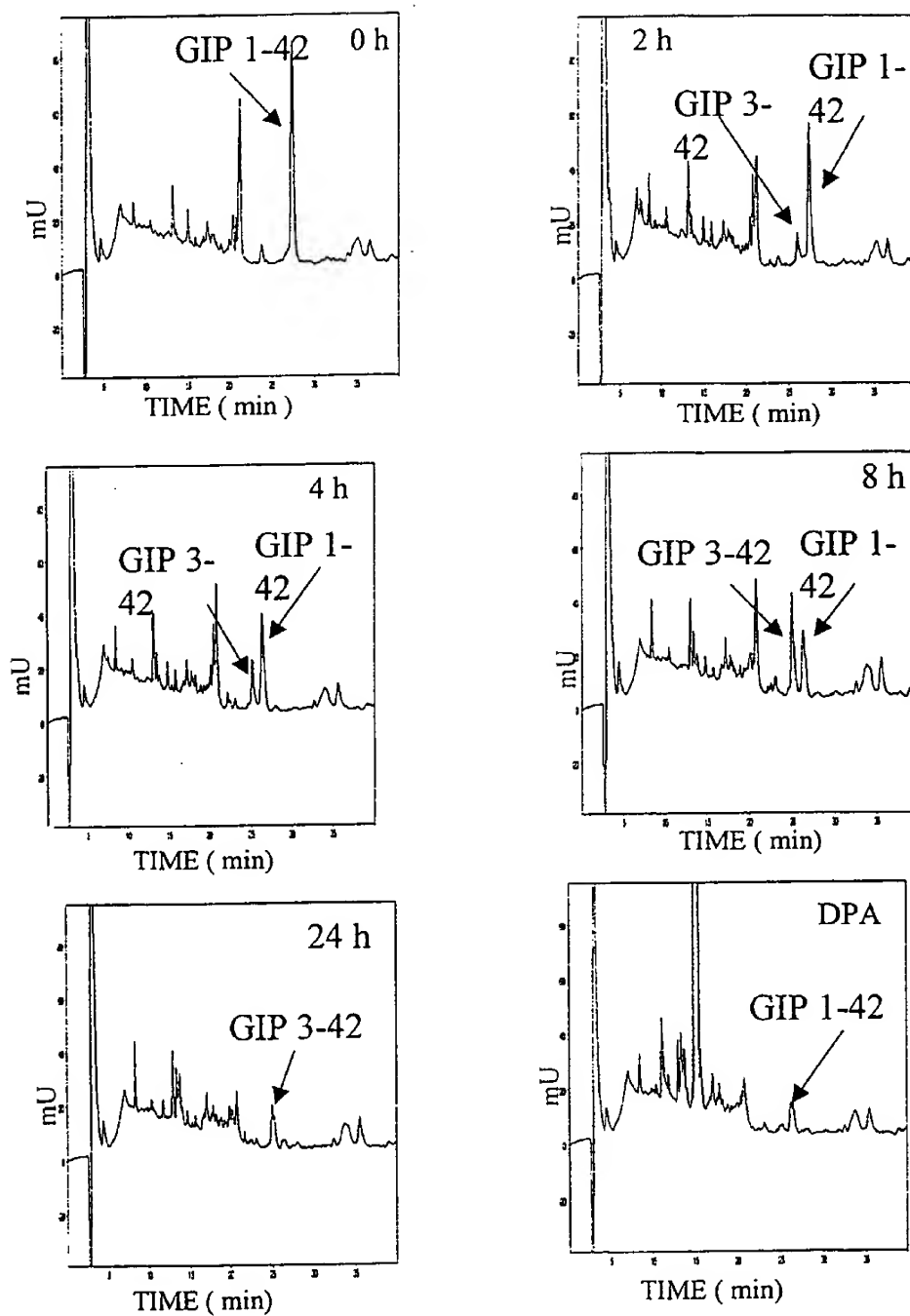


Fig.12. HPLC traces showing human plasma degradation of GIP

WO 00/58360

PCT/GB00/01089

15 / 32

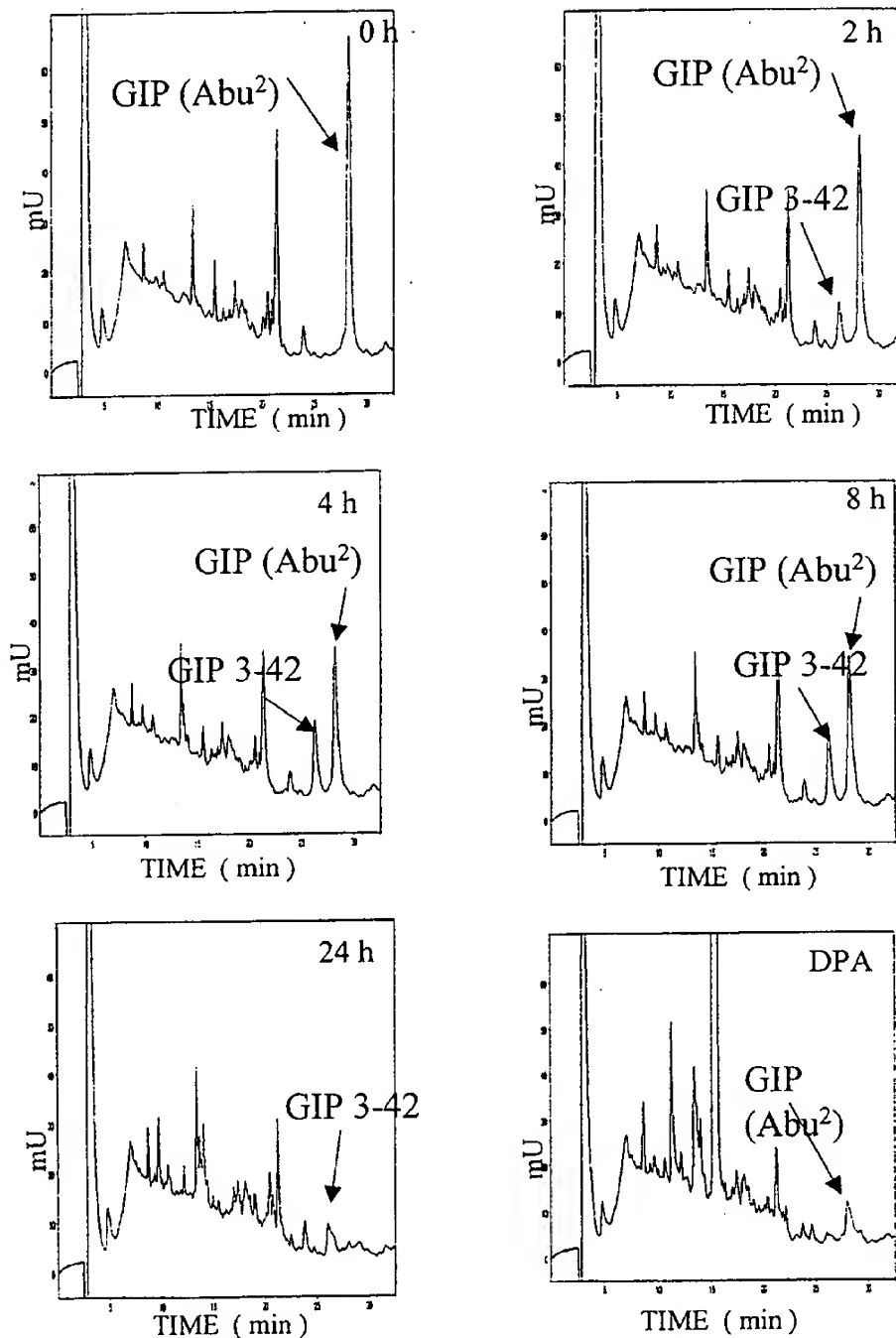


Fig. 13. HPLC traces showing human plasma degradation of GIP (Abu²)

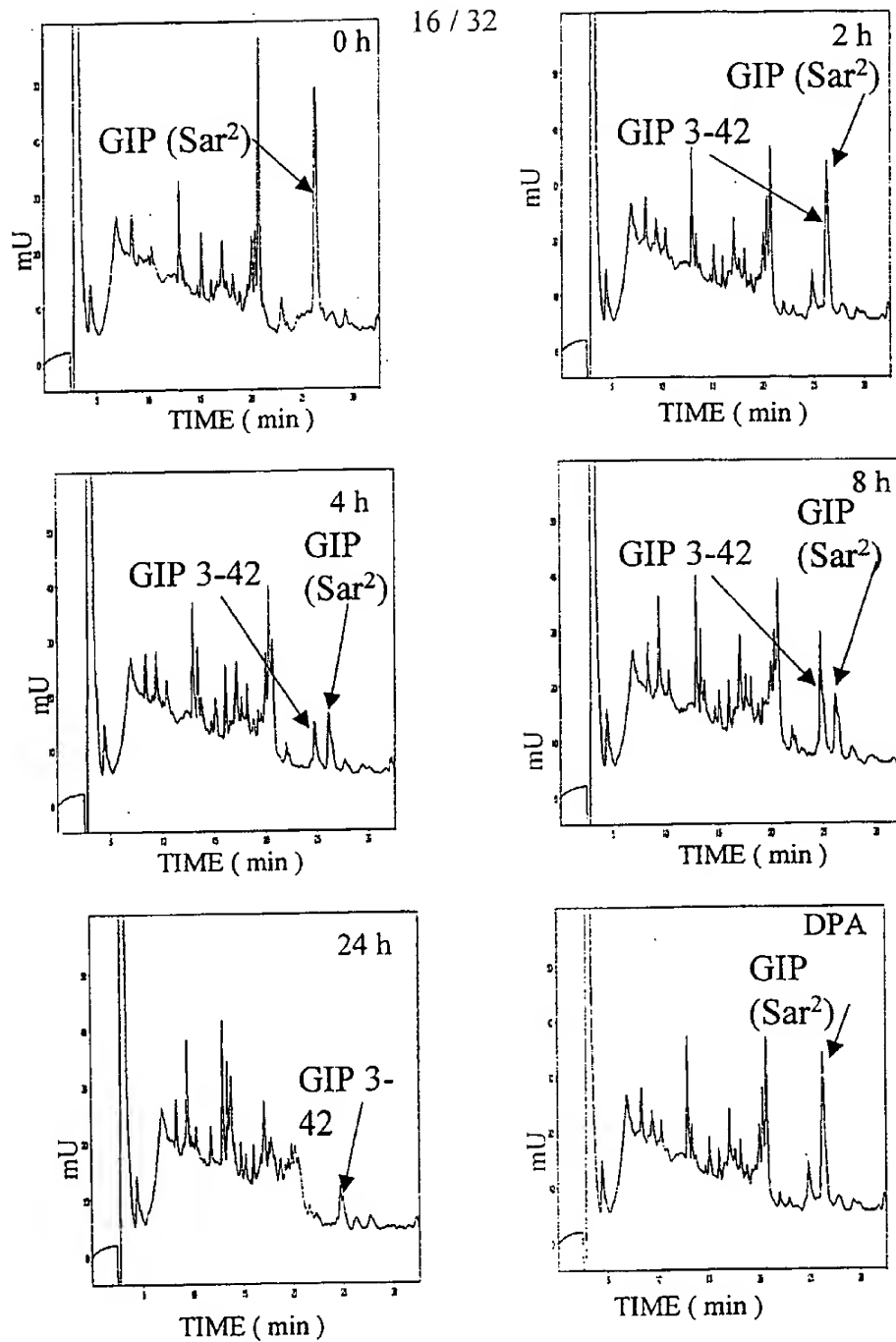


Fig. 14. HPLC traces showing human plasma degradation of GIP (Sar²)

17/32

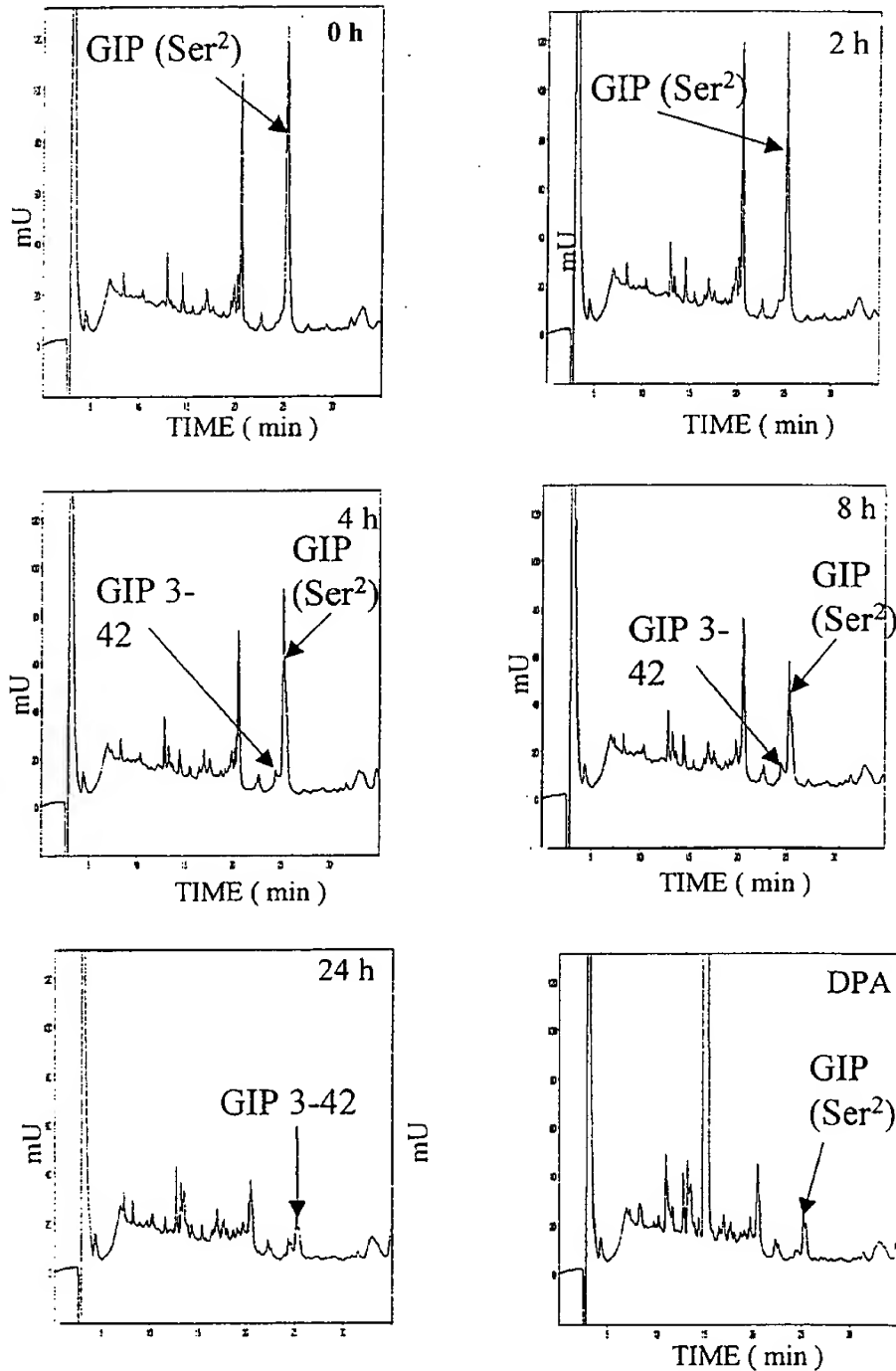


Fig. 15 HPLC traces showing human plasma degradation of GIP(Ser²)

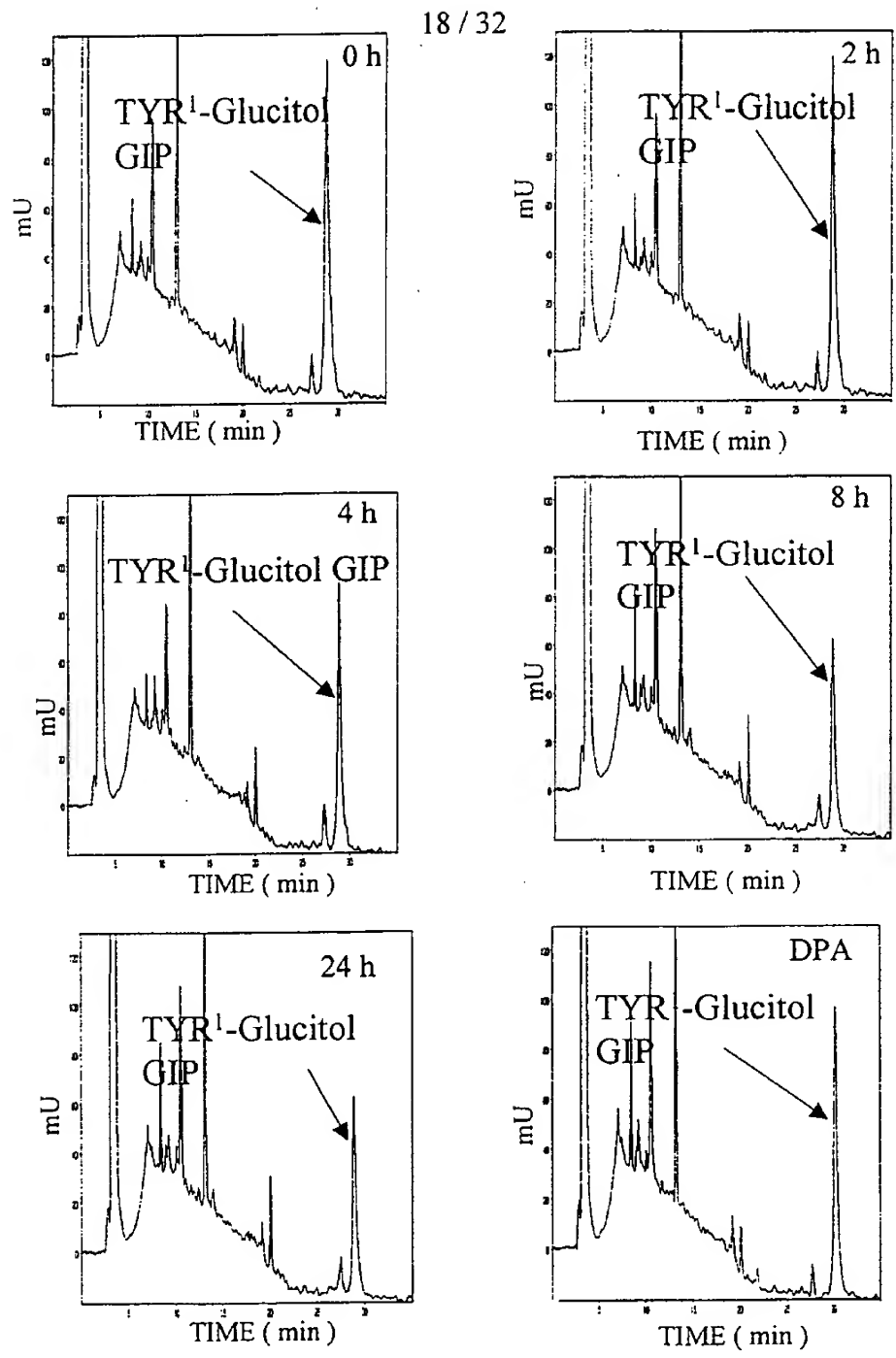
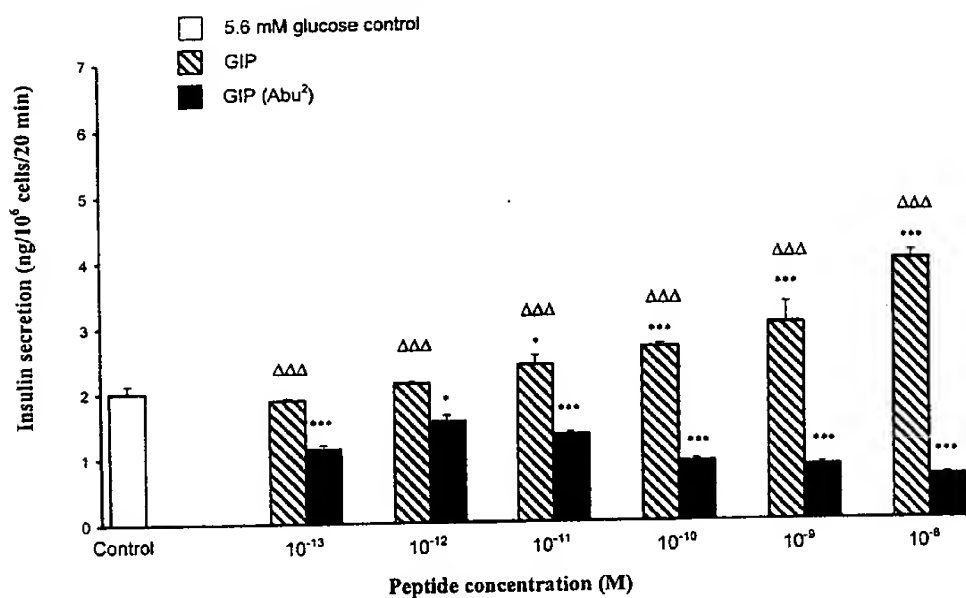


Fig. 16. HPLC traces showing human plasma degradation of glycated GIP

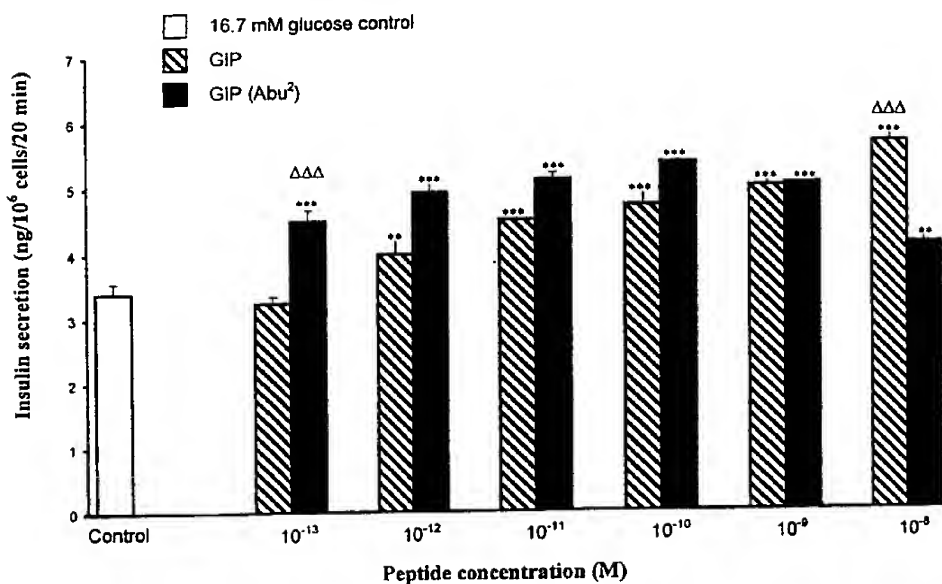
19/32

Fig.17. Graph showing the effects of various concentrations of GIP and GIP (Abu²) on insulin release from BRIN-BD11 cells incubated at 5.6 mM glucose



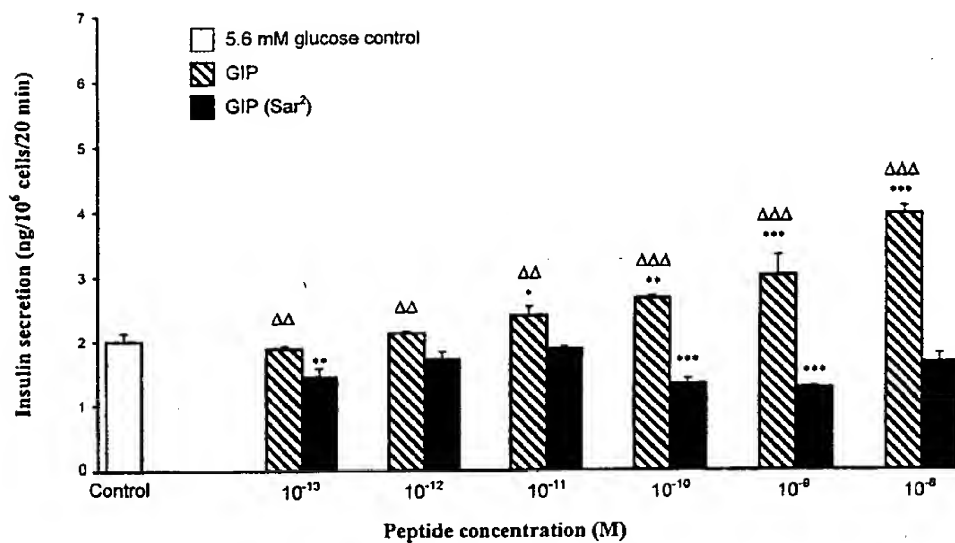
Values are means \pm S.E.M. for 12 separate observations. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ compared to control (5.6mM glucose alone). $\Delta P < 0.05$, $\Delta\Delta P < 0.01$, $\Delta\Delta\Delta P < 0.001$ compared to GIP (Abu²) at the same concentration.

Fig.18. Graph showing the effects of various concentrations of GIP and GIP (Abu²) on insulin release from BRIN-BD11 cells incubated at 16.7 mM glucose:



Values are means ± S.E.M. for 12 separate observations. *P < 0.05, **P < 0.01, ***P < 0.001 compared to control (16.7 mM glucose alone). ΔP < 0.05, ΔΔP < 0.01, ΔΔΔP < 0.001 compared to GIP (Abu²) at the same concentration.

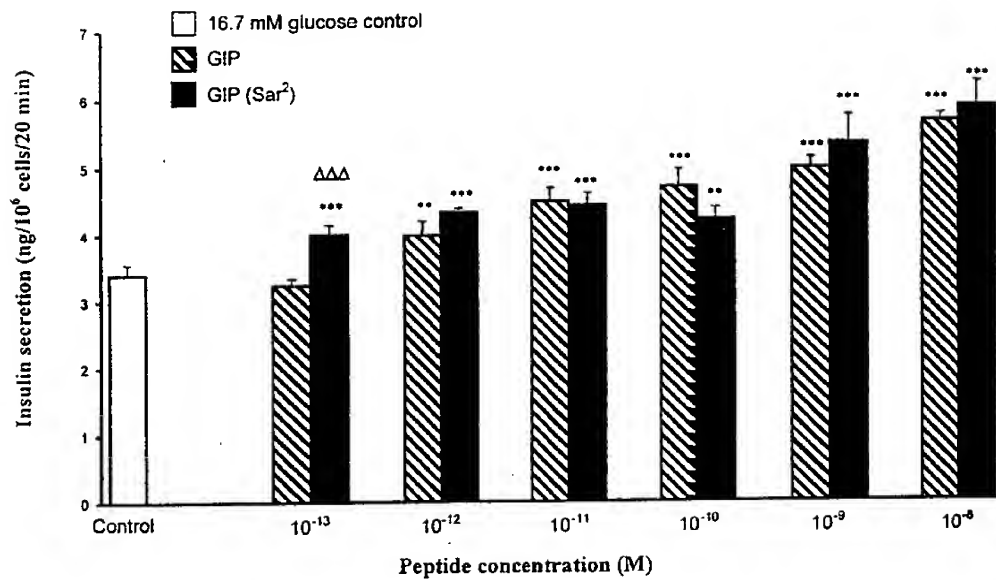
Fig.19. Graph showing the effects of various concentrations of GIP and GIP (Sar²) on insulin release from BRIN-BD11 cells incubated at 5.6 mM glucose



Values are means ± S.E.M. for 12 separate observations. *P<0.05, **P<0.01, ***P<0.001 compared to control (5.6mM glucose alone). ΔP<0.05, ΔΔP<0.01, ΔΔΔP<0.001 compared to GIP (Sar²) at the same concentration.

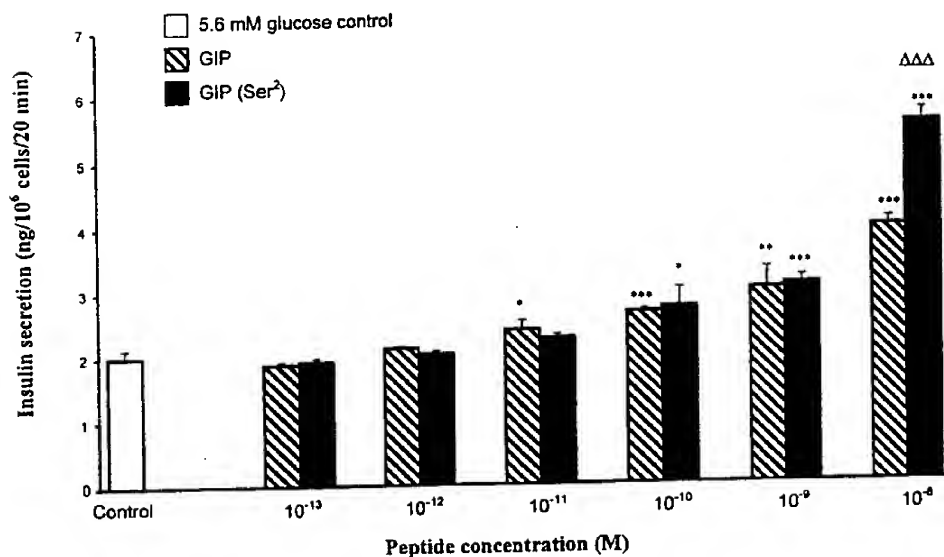
22/32

Fig. 20. Graph showing the effects of various concentrations of GIP and GIP (Sar²) on insulin release from BRIN-BD11 cells incubated at 16.7 mM glucose



Values are means \pm S.E.M. for 12 separate observations. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ compared to control (16.7 mM glucose alone). ^{*} $P < 0.05$, ^{**} $P < 0.01$, ^{***} $P < 0.001$ compared to GIP (Sar²) at the same concentration.

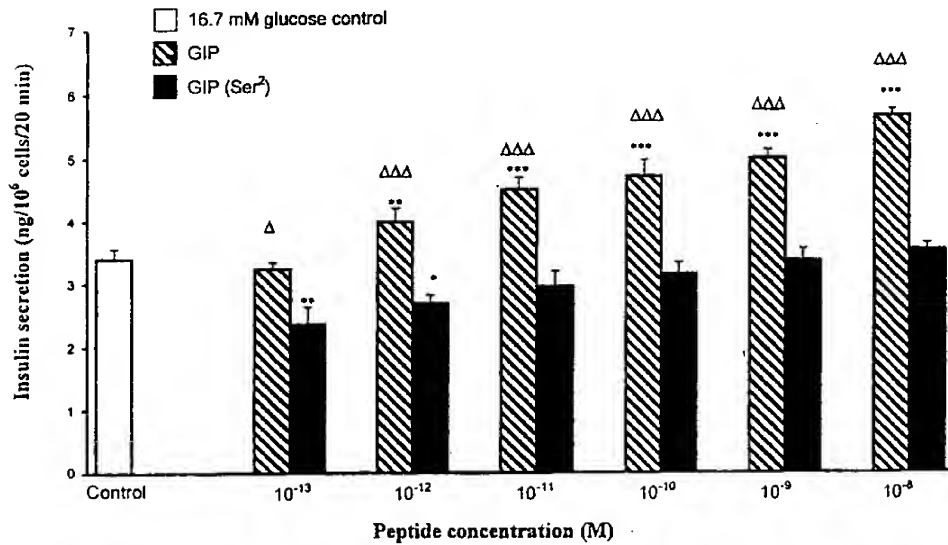
Fig.21. Graph showing the effects of various concentrations of GIP and GIP (Ser²) on insulin release from BRIN-BD11 cells incubated at 5.6 mM glucose



Values are means \pm S.E.M. for 12 separate observations. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ compared to control (5.6mM glucose alone). ^a $P < 0.05$, ^{aa} $P < 0.01$, ^{aaa} $P < 0.001$ compared to GIP (Ser²) at the same concentration.

24/32

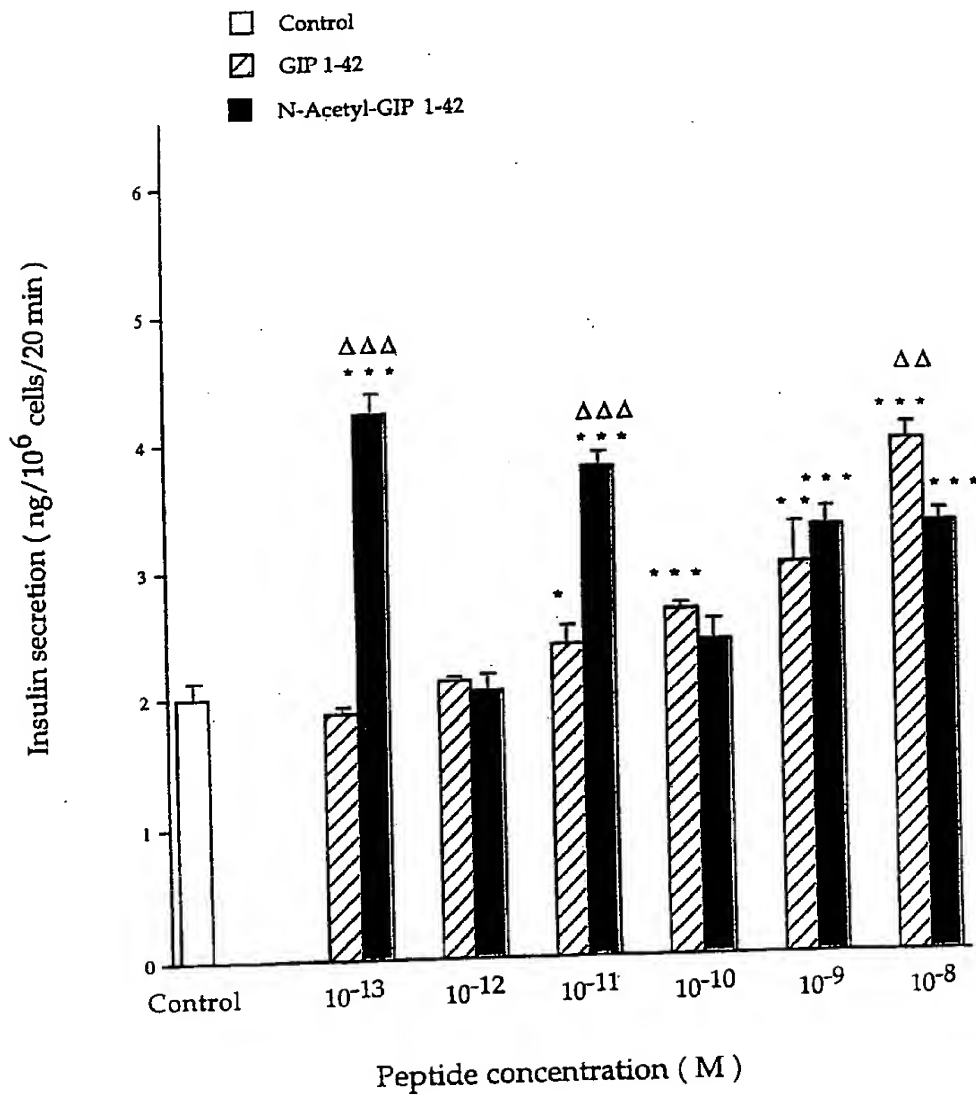
Fig. 22. Graph showing the effects of various concentrations of GIP and GIP (Ser³) on insulin release from BRIN-BD11 cells incubated at 16.7 mM glucose



Values are means \pm S.E.M. for 12 separate observations. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ compared to control (16.7 mM glucose alone). ^Δ $P < 0.05$, ^{ΔΔ} $P < 0.01$, ^{ΔΔΔ} $P < 0.001$ compared to GIP (Ser³) at the same concentration.

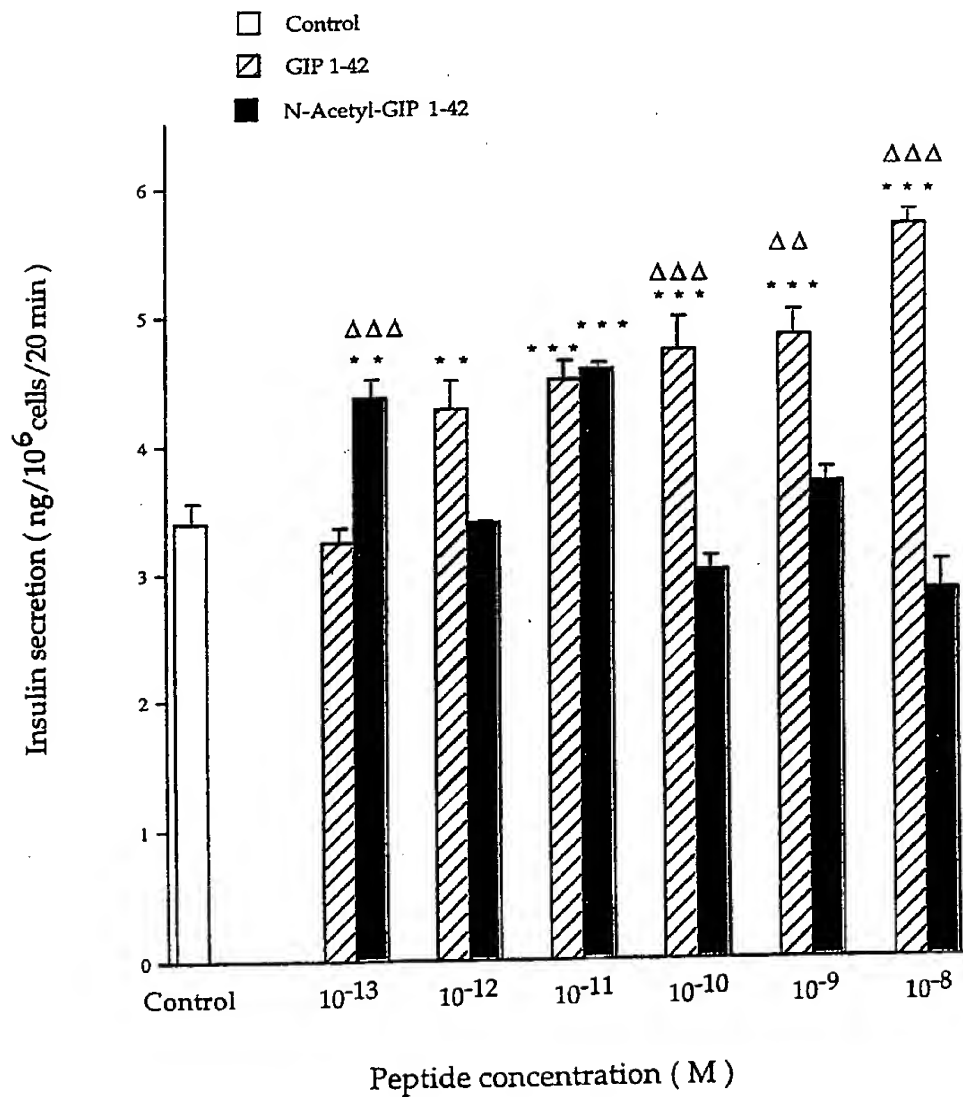
25/32

Fig. 23 Graph showing the effects of various concentrations of GIP 1-42 and N-Acetyl-GIP 1-42 on insulin release from BRIN-BD11 cells incubated at 5.6 mM glucose



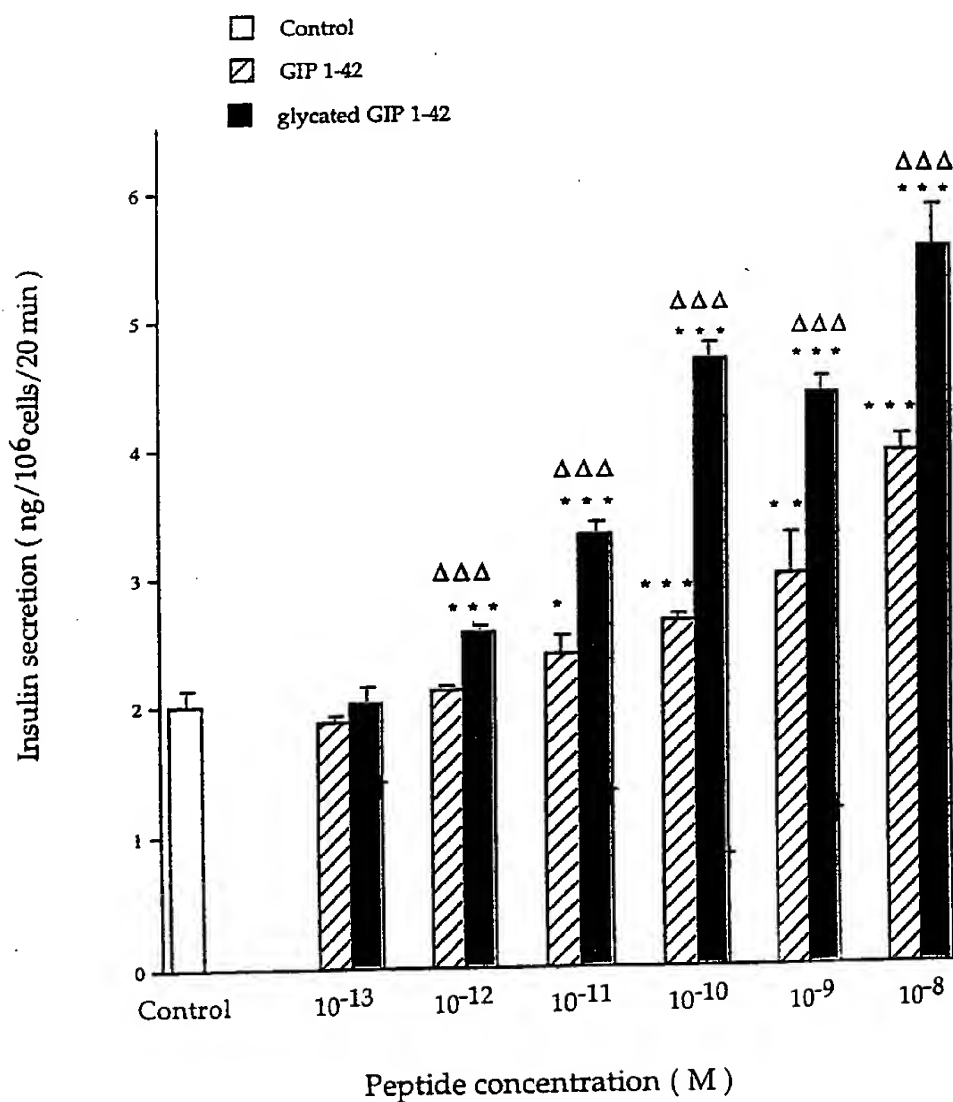
26/32

Fig. 24 Graph showing the effects of various concentrations of GIP 1-42 and N-Acetyl-GIP 1-42 on insulin release from BRIN-BD11 cells incubated at 16.7 mM glucose



27/32

Fig. 25 Graph showing the effects of various concentrations of GIP 1-42 and glycated GIP 1-42 on insulin release from BRIN-BD11 cells incubated at 5.6 mM glucose



28/32

Fig.26 Graph showing the effects of various concentrations of GIP 1-42 and glycated GIP 1-42 on insulin release from BRIN-BD11 cells incubated at 16.7 mM glucose

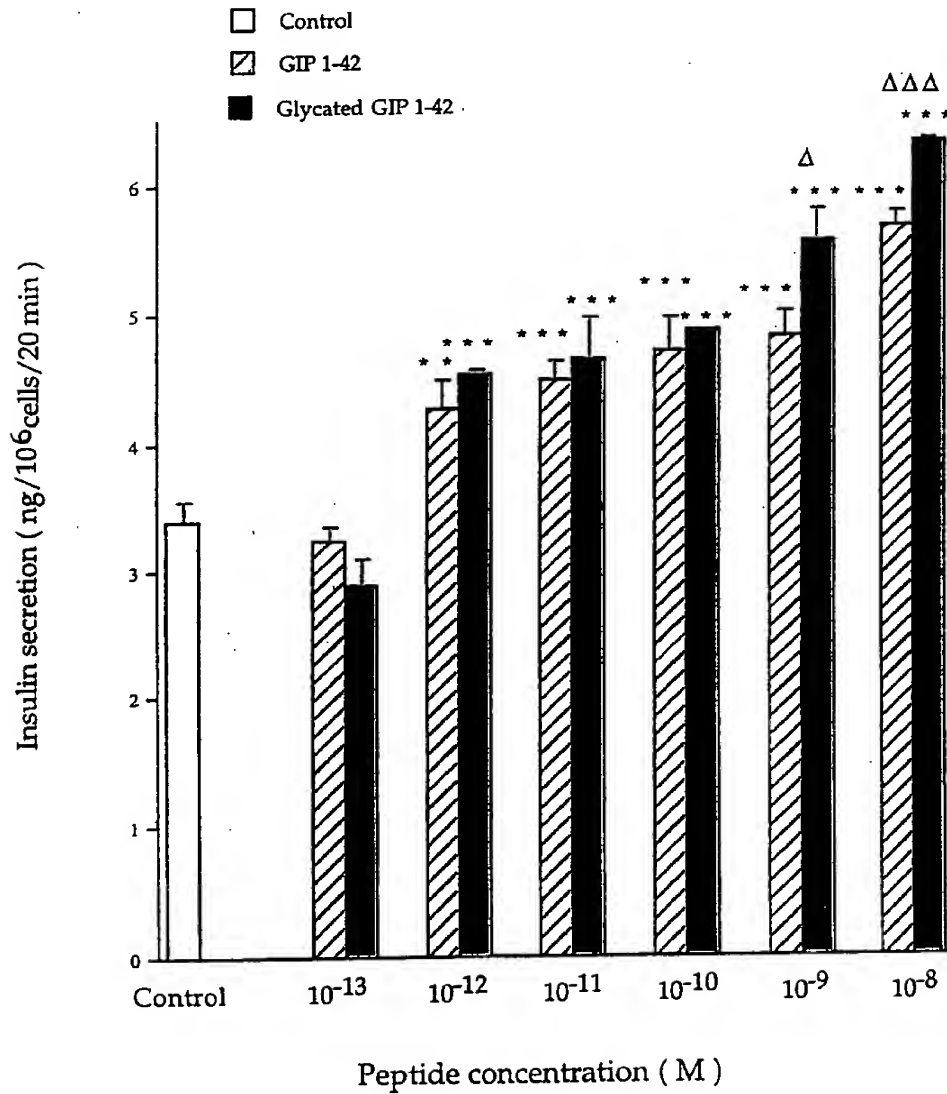
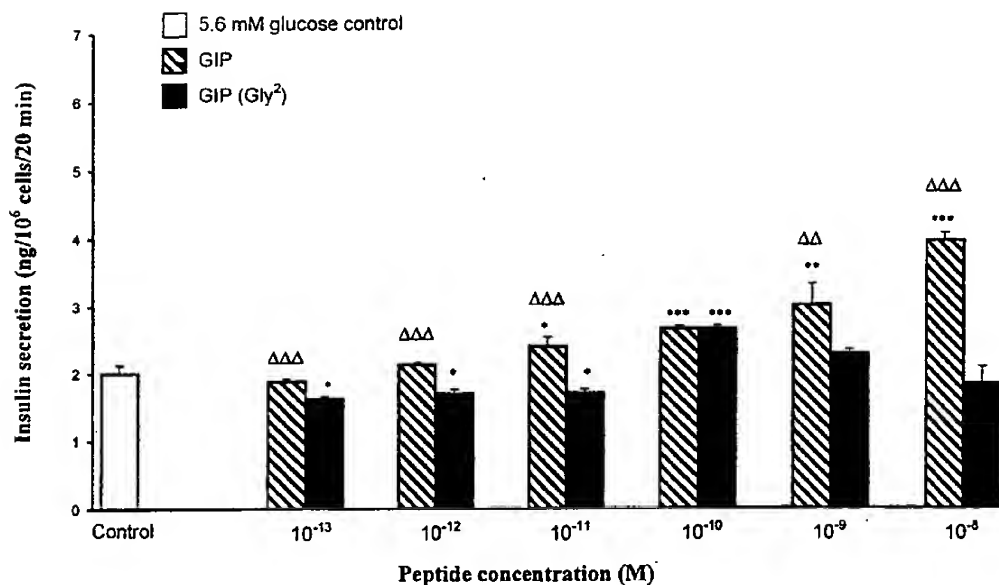


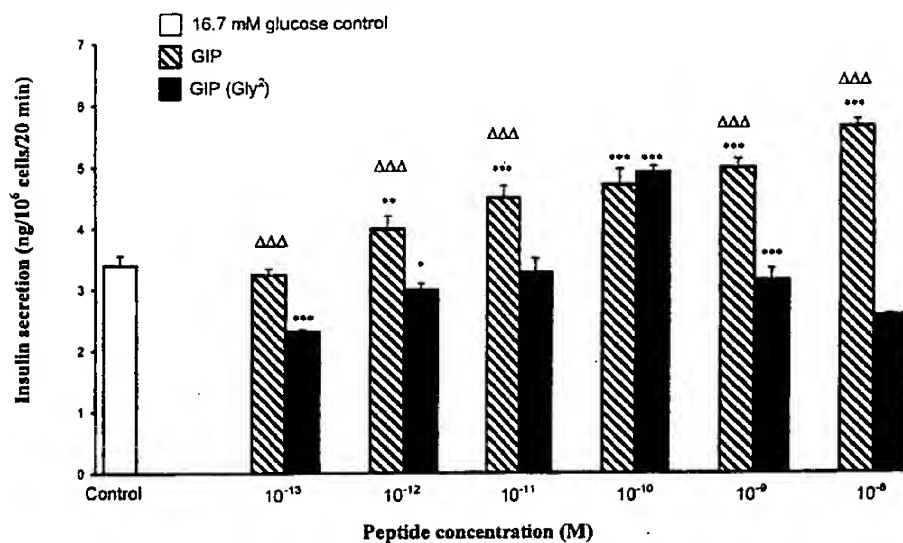
Fig. 27 Graph showing the effects of various concentrations of GIP and GIP (Gly²) on insulin release from BRIN-BD11 cells incubated at 5.6 mM glucose



Values are means \pm S.E.M. for 12 separate observations. *P<0.05, **P<0.01, ***P<0.001 compared to control (5.6mM glucose alone). ΔP<0.05, ΔΔP<0.01, ΔΔΔP<0.001 compared to GIP (Gly²) at the same concentration.

30/32

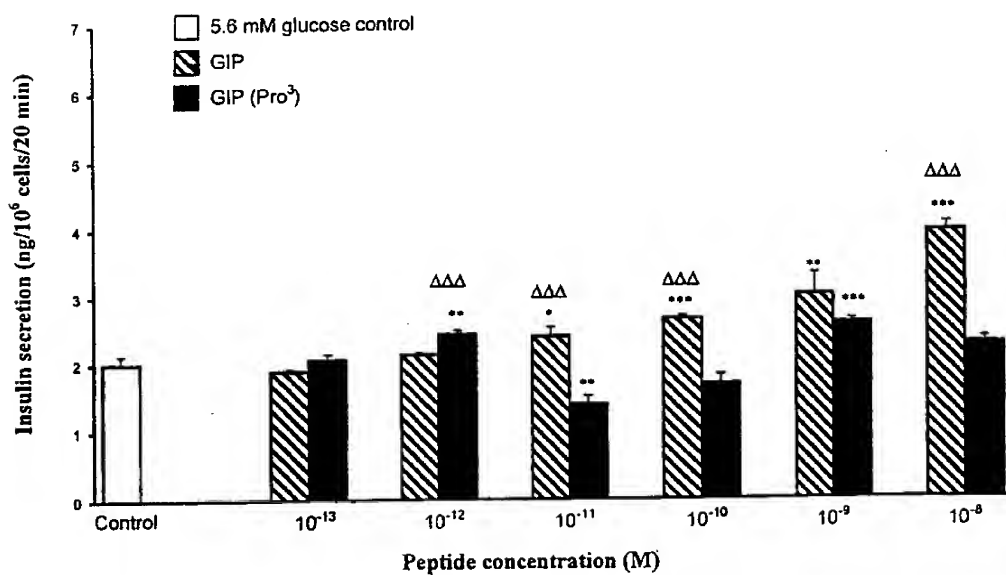
Fig. 28 Graph showing the effects of various concentrations of GIP and GIP (Gly²) on insulin release from BRIN-BD11 cells incubated at 16.7 mM glucose



Values are means \pm S.E.M. for 12 separate observations. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ compared to control (16.7 mM glucose alone). $\Delta P < 0.05$, $\Delta\Delta P < 0.01$, $\Delta\Delta\Delta P < 0.001$ compared to GIP (Gly²) at the same concentration.

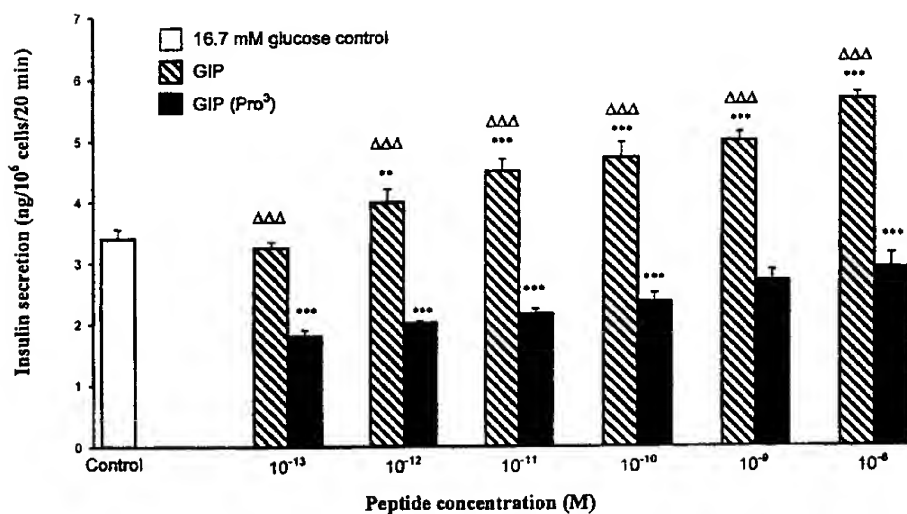
31/32

Fig. 29 Graph showing the effects of various concentrations of GIP and GIP (Pro³) on insulin release from BRIN-BD11 cells incubated at 5.6 mM glucose



Values are means \pm S.E.M. for 12 separate observations. *P<0.05, **P<0.01, ***P<0.001 compared to control (5.6mM glucose alone). ^ΔP<0.05, ^{ΔΔ}P<0.01, ^{ΔΔΔ}P<0.001 compared to GIP (Pro³) at the same concentration.

Fig. 30 Graph showing the effects of various concentrations of GIP and GIP (Pro³) on insulin release from BRIN-BD11 cells incubated at 16.7 mM glucose



Values are means \pm S.E.M. for 12 separate observations. *P<0.05, **P<0.01, ***P<0.001 compared to control (16.7 mM glucose alone). ΔP<0.05, ΔΔP<0.01, ΔΔΔP<0.001 compared to GIP (Pro³) at the same concentration.